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09/666,890	09/20/2000	James L. Hartley	0942.2570003/RWE/DRM	9088

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EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
09/666,890	HARTLEY, JAMES L.	
Examiner	**Art Unit**	
Ethan Whisenant, Ph.D.	1634	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *83-106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *83,84,105 and 106* is/are allowed.

6)☒ Claim(s) *85-1045* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The applicant's Response (filed 08 OCT 02) to the Office Action has been entered. The applicant's response has been entered as paper no. 174. The claims pending in this application are **Claim(s) 83-106.** Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

CLAIM OBJECTIONS

2. Applicant is advised that should Claims 85-89, 97 and 100 found allowable, Claims 95-99 and 101-104 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. Note that Claim 98 is a duplicate of Claim 85, Claim 99 is a duplicate of Claim 86 and Claims 95-97 are duplicates of Claims 87-89. Claim 100 is coextensive in scope with Claims 101-102. Claim 97 is coextensive in scope with Claims 103-104. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless –
>
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** The invention was described in –
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)

35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

CLAIM REJECTIONS UNDER 35 USC § 102/103

5. **Claim(s) 85, 87, 89, 90, 92, 94, 95, 97, 98, 100, 101, 103,** is/are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over The Gibco/BRL Catalog (FEB 1992).

The Gibco/BRL Catalog teaches a kit comprising a 100 bp DNA ladder whose bands can be visualized by ethidium bromide (i.e. EtBR). Note the fragments at 100, 200, and 300 bp. Admittedly, the Gibco/BRL Catalog do not teach using their ladder or to estimate the mass of a nucleic acid. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963). Also, the Gibco/BRL Catalog do not teach making their ladders by the complete digestion of one or more nucleic acid molecules with one or more restriction endonucleases. However, a product is not limited by the why it is made but rather by its structure. If the product in a claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *"In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

6. **Claim(s) 85, 87, 92, 98, 95** is/are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gelfi et al. (1990).

Claim 85 and 98 are each drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 100, 200 and 300 base pairs.

Gelfi et al. teach nucleic acid sequencing ladders comprising fragments of 100, 200 and 300 base pairs. Admittedly, Gelfi et al. do not teach using their ladders as a marker ladder or to estimate the mass of a nucleic acid. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

Claims 87 and 95 are each drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 100, 200 and 300 base pairs.

Gelfi et al. teach nucleic acid sequencing ladders comprising fragments of 100, 200 and 300 base pairs. Admittedly, Gelfi et al. do not teach making their ladders by the complete digestion of one or more nucleic acid molecules with one or more restriction endonucleases. However, a product is not limited by the why it is made but rather by its structure. If the product in a claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *"In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claim 92 drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 100, 200 and 300 base pairs.

Gelfi et al. teach nucleic acid sequencing ladders comprising fragments of 100, 200 and 300 base pairs. Admittedly, Gelfi et al. do not teach using their ladders as a marker ladder or to estimate the mass of a nucleic acid. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re*

Otto , 136 USPQ 458, 459 (CCPA 1963). Also, Gelfi et al. do not teach making their ladders by the complete digestion of one or more nucleic acid molecules with one or more restriction endonucleases. However, a product is not limited by the why it is made but rather by its structure. If the product in a claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *"In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

CLAIM REJECTIONS UNDER 35 USC § 103

7. **Claim(s) 85, 86, 98 and 99** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (1981).

Claim 85 and 98 are each drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 100, 200 and 300 base pairs.

Hartley et al. teach a nucleic acid marker ladder comprising at least 3 nucleic acid fragments. Admittedly, Hartley et al. do not teach that the ladder should comprise at least 3 nucleic acid fragments of 100, 200 and 300 base pairs. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder of Hartley et al. wherein bands of 100, 200 and 300 base pairs are included. The ordinary artisan would have been motivated to modify the method/marker ladder of Hartley et al. in order to estimate the size (i.e. molecular weight) of restriction endonuclease fragments in the range of 100-300 base pairs and in view of the teaching in Hartley et al. who state that "it should be possible to polymerize any DNA segment by this method and "we are currently applying the methods to both larger and smaller DNAs" (see the abstract). It must also be pointed out that Hartley et al. (1981) do not teach using their nucleic acid marker ladder to determine the mass of a nucleic acid in a sample. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

Claim 86 and 99 are each drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 500, 1000 and 2000 base pairs.

Hartley et al. teach a nucleic acid marker ladder comprising at least 3 nucleic acid fragments. Admittedly, Hartley et al. do not teach that the ladder should comprise at least 3 nucleic acid fragments of 500, 1000 and 2000 base pairs. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder of Hartley et al. wherein bands of 500, 1000 and 2000 base pairs are included. The ordinary artisan would have been motivated to modify the method/marker ladder of Hartley et al. in order to estimate the size (i.e. molecular weight) of restriction endonuclease fragments in the range of 500-200 base pairs and in view of the teaching in Hartley et al. who state that "it should be possible to polymerize any DNA segment by this method and "we are currently applying the methods to both larger and smaller DNAs" (see the abstract). It must also be pointed out that Hartley et al. (1981) do not teach using their nucleic acid marker ladder to determine the mass of a nucleic acid in a sample. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

8. **Claim(s) 87-88 and 95-96** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (1981).

Claim 87 and 95 are each drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 100, 200 and 300 base pairs.

Hartley et al. teach a nucleic acid marker ladder comprising at least 3 nucleic acid fragments. Admittedly, Hartley et al. do not teach that the ladder should comprise at least 3 nucleic acid fragments of 100, 200 and 300 base pairs. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder of Hartley et al. wherein bands of 100, 200 and 300 base pairs are included. The ordinary artisan would have been motivated to modify the method/marker ladder of Hartley et al. in order to estimate the size (i.e. molecular weight) of restriction endonuclease fragments in the range of 100-300 base pairs and in view of the teaching in Hartley et al.

who state that "it should be possible to polymerize any DNA segment by this method" and "we are currently applying the methods to both larger and smaller DNAs" (see the abstract). Admittedly, Hartley et al. do not explicitly teach making their ladders by the complete digestion of one or more nucleic acid molecules with one or more restriction endonucleases. However, a product is not limited by the why it is made but rather by its structure. If the product in a claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *"In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claim 88 and 96 are each drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 500, 1000 and 2000 base pairs.

Hartley et al. teach a nucleic acid marker ladder comprising at least 3 nucleic acid fragments. Admittedly, Hartley et al. do not teach that their ladder should comprise at least 3 nucleic acid fragments of 500, 1000 and 2000 base pairs. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder of Hartley et al. wherein bands of 500, 1000 and 2000 base pairs are included. The ordinary artisan would have been motivated to modify the method/marker ladder of Hartley et al. in order to estimate the size (i.e. molecular weight) of restriction endonuclease fragments in the range of 500-2000 base pairs and in view of the teaching in Hartley et al. who state that "it should be possible to polymerize any DNA segment by this method" and "we are currently applying the methods to both larger and smaller DNAs" (see the abstract). Admittedly, Hartley et al. do not explicitly teach making their ladders by the complete digestion of one or more nucleic acid molecules with one or more restriction endonucleases. However, a product is not limited by the why it is made but rather by its structure. If the product in a claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *"In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

9. **Claim(s) 92 and 93** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (1981).

Claim 92 drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 100, 200 and 300 base pairs.

Hartley et al. teach a nucleic acid marker ladder comprising at least 3 nucleic acid fragments. Admittedly, Hartley et al. do not teach that their ladder should comprise at least 3 nucleic acid fragments of 100, 200 and 300 base pairs. However, it would have been *prima facie* obvious to one

of ordinary skill in the art at the time of the invention to modify the method/marker ladder of Hartley et al. wherein bands of 100, 200 and 300 base pairs are included. The ordinary artisan would have been motivated to modify the method/marker ladder of Hartley et al. in order to estimate the size (i.e. molecular weight) of restriction endonuclease fragments in the range of 100-300 base pairs and in view of the teaching in Hartley et al. who state that "it should be possible to polymerize any DNA segment by this method" and "we are currently applying the methods to both larger and smaller DNAs" (see the abstract). Admittedly, Hartley et al. do not teach using their ladders as a marker ladder or to estimate the mass of a nucleic acid. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963). Also, Hartley et al. do not explicitly teach making their ladders by the complete digestion of one or more nucleic acid molecules with one or more restriction endonucleases. However, a product is not limited by the why it is made but rather by its structure. If the product in a claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *"In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claim 93 drawn to a nucleic acid marker ladder comprising at least 3 nucleic acid fragments wherein the size of said at least 3 nucleic acid fragments is 500, 1000 and 2000 base pairs.

Hartley et al. teach a nucleic acid marker ladder comprising at least 3 nucleic acid fragments. Admittedly, Hartley et al. do not teach that their ladder should comprise at least 3 nucleic acid fragments of 500, 1000 and 2000 base pairs. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder of Hartley et al. wherein bands of 500, 1000 and 2000 base pairs are included. The ordinary artisan would have been motivated to modify the method/marker ladder of Hartley et al. in order to estimate the size (i.e. molecular weight) of restriction endonuclease fragments in the range of 500-200 base pairs and in view of the teaching in Hartley et al. who state that "it should be possible to polymerize any DNA segment by this method" and "we are currently applying the methods to both larger and smaller DNAs" (see the abstract). Admittedly, Hartley et al. do not teach using their ladders as a marker ladder or to estimate the mass of a nucleic acid. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative

difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963). Also, Hartley et al. do not explicitly teach making their ladders by the complete digestion of one or more nucleic acid molecules with one or more restriction endonucleases. However, a product is not limited by the why it is made but rather by its structure. If the product in a claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *"In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

10. **Claim(s) 89, 94, 97 and 100** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (1981) as applied against Claims 87-88, 92-93, 95-96, 98-99 above and further in view of the BRL Catalog (1989).

Claim 89 is drawn to an embodiment of Claim 87 or 88 wherein the ladder is stained with ethidium bromide (EtBr). **Claim 94** is drawn to an embodiment of Claim 92 or 93 wherein the ladder is stained with EtBr. **Claim 97** is drawn to an embodiment of Claim 95 or 96 wherein the ladder is stained with EtBr. **Claim 100** is drawn to an embodiment of Claim 98 or 99 wherein the ladder is stained with with EtBr.

As argued above, Hartley et al. reasonably suggests all of the limitations recited in Claim 89, 94, 97, and 100; except these authors do not explicitly teach staining their ladder with EtBr. However, as the use of EtBr for staining nucleic acids was well known and widely practiced at the time of the invention, as evidenced by the BRL Catalog (See especially the legend of the Figure entitled ΦX174 RF DNA / Hae III Fragments on page 317), it would have been, absent an unexpected result, *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder suggested by Hartley et al. wherein the nucleic acid marker ladder is stained with EtBr as suggested by the BRL Catalog. The motivation for modifying the method/marker ladder suggested by Hartley et al. would have been to eliminate the need for radioactive label(s) as taught by Hartley (see Hartley et al. Figure 6 on p. 351).

11. **Claim(s) 101-102** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (1981) as applied against Claims 85-86 above and further in view of the BRL Catalog (1989).

Claim 101 is drawn to a nucleic acid marker ladder comprising all of the limitations set forth in Claim 85 wherein the marker ladder is stained with EtBr. **Claim 102** is each drawn to a nucleic

acid marker ladder comprising all of the limitations set forth in Claim 86 wherein the marker ladder is stained with EtBr.

As argued above, Hartley et al. reasonably suggests all of the limitations recited in Claims 85-86, except these authors do not explicitly teach staining their ladder with EtBr. However, as the use of EtBr for staining nucleic acids was well known and widely practiced at the time of the invention, as evidenced by the BRL Catalog (See especially the legend of the Figure entitled ΦX174 RF DNA / Hae III Fragments on page 317), it would have been, absent an unexpected result, *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder suggested by Hartley et al. wherein the nucleic acid marker ladder is stained with EtBr as suggested by the BRL Catalog. The motivation for modifying the method/marker ladder suggested by Hartley et al. would have been to eliminate the need for radioactive label(s) as taught by Hartley (see Hartley et al. Figure 6 on p. 351).

12. **Claim(s) 103-104** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (1981) in view of the BRL Catalog (1989) as applied against Claim 87-89 above.

Claim 103 is drawn to a nucleic acid marker ladder comprising all of the limitations set forth in Claim 87 wherein the marker ladder is stained with EtBr. **Claim 104** is each drawn to a nucleic acid marker ladder comprising all of the limitations set forth in Claim 88 wherein the marker ladder is stained with EtBr.

As argued above, Hartley et al. reasonably suggests all of the limitations recited in Claims 103-104, except these authors do not explicitly teach staining their ladder with EtBr. However, as the use of EtBr for staining nucleic acids was well known and widely practiced at the time of the invention, as evidenced by the BRL Catalog (See especially the legend of the Figure entitled ΦX174 RF DNA / Hae III Fragments on page 317), it would have been, absent an unexpected result, *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method/marker ladder suggested by Hartley et al. wherein the nucleic acid marker ladder is stained with EtBr as suggested by the BRL Catalog. The motivation for modifying the method/marker ladder suggested by Hartley et al. would have been to eliminate the need for radioactive label(s) as taught by Hartley (see Hartley et al. Figure 6 on p. 351).

13. **Claim(s) 90-91** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (1981) as applied against Claim 87-88 above and further in view of the Stratagene Catalog (1988).

Claim 90 is drawn to a kit comprising a nucleic acid marker ladder as recited in Claim 87. **Claim 91** is drawn to a kit comprising a nucleic acid marker ladder as recited in Claim 88.

As argued above, Hartley et al. reasonably suggests a nucleic acid marker ladder comprising all of the limitations recited in Claims 90 (i.e. Claim 87) and 91 (i.e. Claim 88), except these authors do not explicitly teach placing their nucleic acid marker ladder into a kit . However, as evidenced by the Stratagene Catalog teaching, it was well known at the time of the invention to place the reagents needed to perform a nucleic acid based assay into a kit format. Therefore, absent an unexpected result, it would have been prima facie obvious to the ordinary artisan at the time of the invention to modify the teachings of Hartley et al. with the teachings of the Stratagene Catalog wherein the reagents necessary to perform the method suggested by Hartley et al. are placed into a kit format. The ordinary artisan would have been motivated to make this modification in order to take advantage of the savings and efficiency afforded by kits.

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

14. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection. As regards the new 103 rejections above which rely on Hartley et al. (1981) (i.e. paras 7-9 above) , the examiner now believes that those invention are reasonably suggested (i.e. made *prima facie* obvious) by the teachings of Hartley et al. In summary, it is the examiner's position that in the absence of an unexpected result, it would have been *prima facie* obvious to the ordinary artisan at the time of the invention to include any size DNA fragment(s) in a marker ladder in view of the teaching of Hartley et al. who state that "it should be possible to polymerize any DNA segment by this method" and "we are currently applying the methods to both larger and smaller DNAs" (see the abstract). This teaching would have motivated the ordinary artisan to modify the method of Hartley et al. to produce and utilize other DNA fragments as DNA markers because it was well known at the time of the invention the desirability of markers in the range recited. For example see the legend on page 316 of the BRL Catalog (1992) which teaches "Gibco BRL's "ladders," as unique line of DNA and RNA standards consist of multiple repeats of a nucleic acid sequence. This structure generates a broad, uniform distribution of standard band sizes that facilitates accurate determination of molecular sizes".

ALLOWABLE SUBJECT MATTER

15. **Claims 83-84, and 105-106** are allowable over the prior art of record for the reason(s) of record.

CONCLUSION

16. **Claim(s) 83-84, and 105-106** is/are allowable while Claim(s) 85-104 is/are rejected and/or objected to for the reason(s) set forth above.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.

Ethan Whisenant, Ph.D.
Primary Examiner